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www.jkns.or.kr 10.3340/jkns.2009.46.2.123

Print ISSN 2005-3711 On-line ISSN 1598-7876

J Korean Neurosurg Soc 46 : 123-129, 2009

Clinical Article

Incidence and Risk Factors of Infection Caused by Vancomycin-Resistant Enterococcus Colonization in Neurosurgical Intensive Care Unit Patients

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Objective : This study was aimed to identify the incidence and risk factors of *vancomycin-resistant enterococcus* (VRE) colonization in neurosurgical practice of field, with particular attention to intensive care unit (ICU).

Methods : This retrospective study was carried out on the Neurosurgical ICU (NICU), during the period from January. 2005 to December. 2007, in 414 consecutive patients who had been admitted to the NICU. Demographics and known risk factors were retrieved and assessed by statistical methods.

Results : A total of 52 patients had VRE colonization among 414 patients enrolled, with an overall prevalence rate of 6.1%. *E. faecium* was the most frequently isolated pathogen, and 92.3 % of all VRE were isolated from urine specimen. Active infection was noticed only in 2 patients with bacteremia and meningitis. Relative antibiotic agents were third-generation cephalosporin in 40%, and vancomycin in 23%, and multiple antibiotic usages were also identified in 13% of all cases. Multivariate analyses showed Glasgow coma scale (GCS) score less than 8, placement of Foley catheter longer than 2 weeks, ICU stay over 2 weeks and presence of nearby VRE-positive patients had a significantly independent association with VRE infection.

Conclusion : When managing the high-risk patients being prone to be infected VRE in the NICU, extreme caution should be paid upon. Because prevention and outbreak control is of ultimate importance, clinicians should be alert the possibility of impending colonization and infection by all means available. The most crucial interventions are careful hand washing, strict glove handling, meticulous and active screening, and complete segregation.

KEY WORDS : Glasgow coma scale score · Intensive care unit · Neurosurgery · Segregation · Vancomycin-resistant enterococcus.

INTRODUCTION

First identified in 1986, *vancomycin-resistant enterococcus* (VRE) has rapidly become one of the leading causes of nosocomial infection and major growing problems in health care facilities globally[9,13]. The incidence and prevalence of VRE colonization, either clinically evident or latent however, vary widely among hospitals. During several years of the last decade, identification of VRE isolates was much increased in all hospital groups, with 2% to 16% prevalence[11]. In the United States, up to 53% rates have been reported in the largest teaching hospitals[23]. Studies have suggested that such VRE rates are highest among critically ill patients specifically those in the intensive care units (ICUs), for whom limited treatment options are available[1,9,13].

Such an increasing outburst of VRE colonization is generally attributed to frequent exposure to antimicrobial agents, particularly the use of cephalosporin and vancomycin, decreased immunity or neutropenia, hepatic or renal insufficiency, use of steroids and / or antacids, proximity to other patients with VRE, severity of underlying diseases, particularly hepato-renal insufficiency, prior surgery, a low albumin level, invasive procedure or treatment, and prolonged hospital stays[2-4,19]. Once colonized by VRE, a person has 5- to 10- fold increased risk of developing severe infection[16].

Most VRE infections occur when enterococci are intro-

• Received : March 12, 2009 • Revised : June 22, 2009
• Accepted : August 5, 2009
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duced into normally-sterile sites such as blood and urine. VRE infections are associated with increase of clinical infectious diseases as followings; endocarditis, urinary infections, peritonitis, vascular sepsis, and wound infections. However, the role of VRE for increasing infectious disease is still uncertain[16].

Characteristics of neurosurgical patient cohorts, especially in the ICU setting, where many unconscious patients harboring several life-supporting catheters, drains and monitoring devices, being totally dependent upon medical personnel's surveillance make them remarkably susceptible to bacterial super-infection. With regard to this second-hand infection issue, there are practically no literatures in the neurosurgical field. We found only one relevant paper in English language[18].

The aim of the present study is herein, to identify incidence and risk factors of VRE in neurosurgical practice with utmost emphasis on the ICU setting. In doing so, preventive measures and therapeutic protocols can be sought and discussed.

MATERIALS AND METHODS

Patients

This retrospective observational study was carried out on in-patients of the neurosurgical department at our institute, facilitating 15 ICU beds and 70 beds in the Neurosurgical Ward, respectively. During the recent three years, from January 2005 to December 2007, a total of 3,736 consecutive patients were admitted to our department. And, during the same time period, a total of 851 patients were also admitted and were treated at the Neurosurgical ICU (NICU). In a whole, VRE colonization was serologically confirmed in 56 patients regardless of their clinical manifestation. Prior to this period, only 3 cases of sporadic VRE infection were reported, and therefore, they were discarded from this study.

Among 851 patients who had been admitted to the ICU, 201 patients died either due to direct neurological insult, concomitant or complicated medical illness : 129 patients within two weeks post-admission, and 72 patients beyond 2 weeks. This made a total of 650 patients admitted in the ICU. Of these 650 patients, 236 patients were excluded due to referral to the other hospital or other department (n = 105), insufficient patient data (n = 98), or repeated ICU admission under either the same diagnosis or different illness (n = 32). Consequently, subtotal of 414 patients were enrolled in this study, a cohort composed of 362 patients as a control group without VRE colonization and 52 patients who became exclusively infected during ICU stay. Four patients who were infected by VRE during the general ward admission were discarded (Fig. 1).

Collected data regarding these patients included as followings : demographic information, primary neurosurgical diagnosis at discharge (according to International Classification of Disease, 10th ed., ICD-10), underlying medical co-morbid disease, serious interim medical illness, invasive procedure or numbers and days of indwelling catheters or tubes, Glasgow coma scale (GCS) score, use of antibiotics, use of mechanical ventilator, days in the ICU or other ward in the hospital, and use of antibiotic agents.

Three types of specimen (stool, sputum, and urine) were collected from each patient once a week during the admission, on every Monday morning. Patients were considered to be colonized if VRE was identified in at least 1 sample. All patients with VRE isolation were segregated and isolated in designated room for until at least 3 weeks of consecutive negative culture.

Microbiological methods

Vancomycin resistance was determined using the following method : specimens were plated onto the Mueller-Hilton or brain-heart infusion agar already impregnated with vancomycin (2 and 4 ug/mL). Positive plates were then, further assessed using an Etest® (AB Biodisk, Solna, Sweden) to determine the minimum inhibitory concentration (MIC) of the organism. The organism was cultured on strips, and on teicoplanin strips to identify vanA phenotypes for up to 48 hours. The following criteria were used to define vancomycin resistance : MIC of 4 ug/mL is classified as sensitive, MIC of > 8-16 ug/mL as intermediate, and MIC of > 32 ug/mL as resistant.

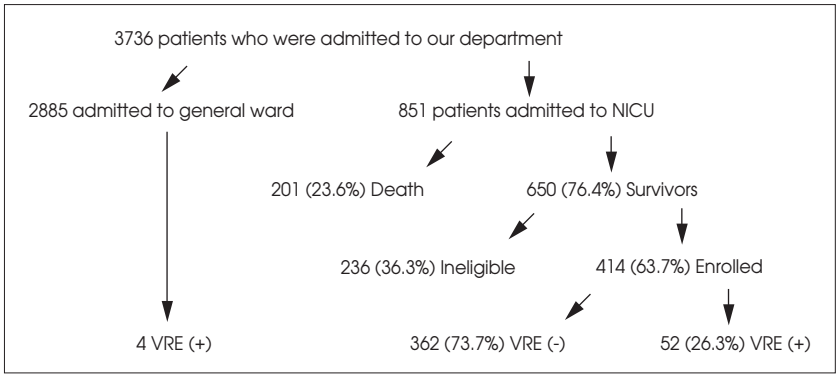

Fig. 1. Flow sheet of patients enrolled in this study. NICU : Neurosurgical intensive care unit, VRE : vancomycin-resistant enterococci

Statistical analysis

Continuous variables were expressed as mean ± standard deviation, and categorical variables as percentages. The chi-square test and Student t-test were first used where appropriate, significance was set at a probability value of 0.05, and 95% of confidence interval (CI) were calculated. By utilizing personal statistical software, SPSS 13 (SPSS Inc., Chicago, Il, USA), univariate and multivariate analyses were con-ducted. The univariate analysis was performed to identify risk factors for VRE colonization, and then multivariate analysis was done to calculate the odds ratio and 95% CIs. Statistical methods applied herein, were backward elimination manner to control confounding, because we started working from the largest model to the smallest one. Factors that were neither associated in univariate analysis in our study nor in the literature as risk factors have been excluded. In this way, a stepwise multiple logistic regression method was used.

RESULTS

Incidence and demographics

Fifty-two patients with VRE colonization had previous history of ICU admission, while only four patients had no history of ICU admission (n = 3) or direct admission to the general ward (n = 1). The overall incidence of VRE infection in the whole patients (n = 3736) was 1.5%, and the incidence was further decreased to 0.14% when assessed in non-ICU patients (4 out of 2885). This incidence however, was sharply elevated to 6.1%, if cohort was confined to the ICU patients (52 out of 851). The mean age was 58.36 ± 15.35 years (range, 25-88 years), and there was female preponderance with a gender ratio of 1.3 : 1 (56% : 44%).

The mean duration of total hospitalization before VRE isolation was 73.30 ± 56.74 days (range, 9-573 days), and it was mainly attributed to three patients who had lengthy admission greater than 365 days. If these three patients were excluded from the data, mean duration was decreased to 35.80 ± 12.41 days. More importantly, the mean duration of ICU stay before VRE isolation was 13.90 ± 3.82 days (range, 9-25 days). And, the mean period required for isolation was 37.2 ± 16.44 days (range, 26-102 days).

The most frequent underlying diseases were diabetes mellitus and hypertension, both of which were present in 27 (51.9%) patients. Sixty-five percent of patients with VRE isolation had initial GCS score of below 8. The leading cause of hospitalization, according to the ICD-10, was cerebrovascular diseases, regardless of surgical intervention, representing 48.1% of all.

Recurrent VRE isolation was noted in two patients. Eight of 52 patients (13.5%) who were included in the present

Table 1. Bivariate analysis according to mean value of baseline characteristics of patients enrolled (n = 414)

Data	Number of cases VRE (+) (n = 52)	*p*	Number of patients VRE (-) (n = 362)	*p*
Sex (M : F)	23 : 29 (44% : 56%)	> 0.05	175 :187 (48% : 52%)	> 0.05
Age	58.36 ± 15.35 (25-88)	> 0.05	56.72 ± 24.51 (14-91)	> 0.05
Duration of hospitalization	73.30 ± 56.74 (9-573)	0.001	58.81 ± 20.55 (5-728)	> 0.05
before VRE isolation*	35.80 ± 12.41 (9-186) †	> 0.05		
Duration of ICU stay before VRE isolation*	13.90 ± 3.82 (9-38)	> 0.05	11.50 ± 5.82 (5-36)	> 0.05
Therapeutic isolation period	37.20 ± 16.44 (26-102)	> 0.05	N/A	N/A
Underlying medical illness ‡		> 0.05		> 0.05
Diabetes mellitus	16 (30.8%)		72 (19.9%)	
Hypertension	16 (30.8%)		93 (25.7%)	
Pneumonia	9 (17.3%)		28 (7.7%)	
Renal disease	6 (11.5%)		41 (11.3%)	
Hepatopathy	5 (9.6%)		68 (18.8%)	
Others	14 (26.9%)		102 (28.2%)	
Primary neurosurgical illness§		> 0.05		> 0.05
Cerebrovascular diseases	25 (48.1%)			
Traumatic brain injury	20 (38.4%)			
Brain tumor	5 (9.6%)			
Spine diseases	2 (3.8%)			
GCS score on admission		> 0.05		> 0.05
13-15	8 (15.4%)		172 (47.5%)	
9-12	10 (19.2%)		138 (38.1%)	
< 8	34 (65.4%)		52 (14.4%)	
No. of indwelling catheter	4.6 (4-7)	> 0.05	3.8 (3-7)	> 0.05
Foley catheter > 14 days	42	> 0.05	82	> 0.05
Interim medical illness (+)	28		145	
Mechanical ventilation (+)	23		47	
Recurrence	2/56	-10 [6]	N/A	N/A
Mortality	8	> 0.05	19	> 0.05

*In VRE (+) group, mean duration denotes elapsed days before pathogen isolation, whereas in VRE (-) group, mean duration denotes total admission days, †Mean hospitalizing duration, if three patients whose admission was greater than 365 days were excluded from the data, ‡Renal diseases include chronic renal failure (4), and acute renal failure (2). Hepatopathy includes liver cirrhosis (3) and acute hepatitis (2). Others include atrial fibrillation, pulmonary edema, angina, myocardial infarction, cellulitis, meningitis, and malignancy, §Cerebrovascular diseases include subarachnoid hemorrhage (12), intracerebral and/or intraventricular hemorrhage (12), and cerebral infarction (1). Spine diseases encompass. GCS : Glasgow coma scale, ICU : intensive care unit, N/A : not applicable, VRE : *vancomycin-resistant enterococcus*

study died, but none of the deaths was directly attributable to a VRE infection (Table1).

Microbiological results

With regard to the pathogens, eighty-two percent of all VRE isolates were *E. faecium*. *E. gallinarum* colonization accounted for 10% of all patients (6 patients), and *E. faecalis* and *E. casseliflavus*, each from two patients (4%) (Table 2). Table 2 also shows the principal sites from which VRE was isolated. Ninety-two percent (48 out of 52 patients) of all VRE were isolated from urine specimen, and remaining 8% (4 out of 52) of VRE were isolated from blood, stool, and cerebrospinal fluid, respectively. Only two isolates were obtained from active infections, such as meningitis and bacteremia. And, only these two patients were treated by systemic linezolid (Zyvox™) administration.

The use of all antibiotic agents within 30 days of culture, longer than at least 7 days were recorded, focusing on vancomycin, third-generation cephalosporins, and concurrent use of the 2 or more agents. Third-generation cephalosporin was the most frequently used antibiotics (58%), and vancomycin in 19% of patients with VRE isolation. Among 52 patients, 24 patients were treated by more than three antibiotics (Table 3).

Risk factors for VRE infection

The univariate analysis shows that female gender, GCS score on admission less than 9, co-morbid diabetes, intervening episode of lung infection, number of indwelling catheters more than 4 lines, mechanical ventilation and ICU stay longer than 2 weeks, and presence of nearby VRE-positive patients were all associated with VRE infection (Table 4). On the other hand, age, duration of whole hospitalization prior to VRE identification,

Table 2. Enterococcal strain species according to the site of isolation*

Species	No of isolates					
	Urine	Blood	Stool	CSF	Pus	Total
E. faecium	40 (1)	1 (1)	1	1	0 (1)	43 (3)
E. gallinarum	5 (1)	0	0	0	0	5 (1)
E. faecalis	1	1	0	0	0	2
E. casseliflavus	2	0	0	0	0	2
Total	48 (2)	2 (1)	1	1	0 (1)	52 (4)

*Numbers in parentheses represent those of 4 patients not infected in the NICU. CSF : cerebrospinal fluid, NICU : Neurosurgical intensive care unit

Table 3. Antibiotic agents used prior to VRE identification

Antibiotics	No of cases (%)	
Third-generation cephalosporin	21/52 (40.4)	2 / 4*
Vancomycin	12/52 (23.1)	1 / 4*
Metronidazole	4/ 2 (7.7)	1 / 4*
Fourth generation cephalosporin	3/52 (5.8)	
More than 2 antibiotic	5/52 (9.6)	
More than 3 antibiotics	7/52 (13.5)	

*Denote numbers of 4 patients not infected in the NICU. NICU : Neurosurgical intensive care unit, VRE : *vancomycin-resistant enterococcus*

Table 4. Univariate analysis for factors associated with VRE infection

Variables	*p*-value	OR (95% CI)
Gender		
Male		
Female	0.021	2.75 (1.17-4.18)
GCS score		
13-15		
9-12		
< 8	0.00001	18.2 (3.55-26.67)
Medical co-morbidity		
Diabetes	0.015	1.73 (1.02-3.25)
Renal disease		
Hepatopathy		
Pneumonia		
Interim lung infection		
Yes		
No	0.001	4.24 (2.01-7.58)
Number of indwelling catheters		
1-3		
> 4	0.038	1.52 (1.07-2.23)
Mechanical ventilation		
< 2 weeks		
> 2 weeks	0.005	4.17 (2.61-8.59)
ICU stay		
< 2 weeks		
> 2 weeks	0.01	2.83 (1.26-4.11)
Previous antibiotics coverage		
Vancomycin		
Cephalosporin		
Presence of nearby VRE (+) patient		
Yes	0.0001	7.66 (1.59-12.37)
No		

Only statistically significant values are expressed. GCS : Glasgow coma scale, ICU : intensive care unit, OR : odds ratio, VRE : *vancomycin-resistant enterococcus*

Table 5. Independent risk factors after multivariate analysis for VRE infection

Variables	*p*-value	OR (95% CI)
Female gender	0.10	1.83 (0.77-1.86)
GCS score ≤ 8	0.01	2.27 (1.45-2.99)*
Co-morbid diabetes (+)	0.05	1.54 (0.91-2.06)
Interim lung infection (+)	0.08	1.23 (0.71-1.89)
Indwelling catheters > 4	0.25	1.07 (0.73-1.66)
Foley catheter > 2 weeks	0.001	2.34 (1.27-2.74)*
Mechanical ventilation > 2 weeks	0.5	0.83 (0.51-1.22)
ICU stay > 2 weeks	0.03	1.71 (1.15-2.31)*
Use of vancomycin / cephalosporin	0.08	1.41 (0.92-3.17)
Presence of nearby VRE (+) patient	-10^5	3.18 (1.81-8.70)*

*Statistically significant. GCS : Glasgow coma scale, ICU : intensive care unit, VRE : *vancomycin-resistant enterococcus*

primary neurosurgical illness, antibiotic agents used, and final outcome were not significantly associated with VRE infection.

Multivariate analysis shows some predictive independent risk factors for VRE infection (Table 5). These are GCS score less than 8, Foley catheter placed longer than 2 weeks, ICU stay over 2 weeks, and presence of nearby VRE-positive patients. Interestingly enough, use of third-generation cephalosporin and vancomycin did not show any statistical significance.

DISCUSSION

General overview of VRE infection

Some enterococci have been recently emerged as important nosocomial pathogens because of their innate resistance to several classes of antibiotics and their ability to acquire additional resistance markers[2]. Resistance to glycopeptides constituting vancomycin is the last but not the least of the markers acquired[2]. In case-control study however, colonization and infection with VRE have been associated with exposure to not only vancomycin, but also third-generation cephalosporin, antibiotics active against anaerobes, ciprofloxacin, and aminoglycosides[8,19]. The microbiological basis for association between such antibiotic exposure and VRE isolation is not well defined yet. Vancomycin exposure seems to exert selective pressure and to disrupt on the intestinal colonizing bacteria favoring the proliferation of the VRE, an opportunistic pathogen. It is reported that VRE-colonized patients who received anti-anaerobic antibiotics (Metronidazole) have increased VRE density in stool[5]. The VRE therefore, most frequently colonized in the gastrointestinal tract and the skin, and are able to survive in the environment. In this point of view, transmission of VRE is deemed to occur through direct contact with colonized or infected patients, through indirect contact via hands of health-care workers, or via contaminated patient-care equipment or environmental surfaces[19].

Vancomycin resistance has been classified into five phenotypes, VanA to VanE. Of these, only the phenotype VanC is intrinsically present in two species (*E. gallinarum* and *E. casseliflavus*). All the others are acquired in the two principal species (*E. faecalis* and *E. faecium*)[8]. Strains of *Enterococcus faecium* predominate among VRE, with an average of 50% showing resistance to vancomycin. Although *Enterococcus faecalis* is the most prevalent of all enterococci caus-ing infections, more recent data show an increase in the proportion of infections caused by *E. faecium*, ranging from 15% to 20%[15,17].

The first guidelines for the control of VRE in hospitals were published in 1994 by the Center for Disease Control (CDC) Hospital Infection Control Practices Advisory Committee (HICPAC)[10]. The control measures to reduce cross transmission among hospitalized patients are restriction of vancomycin use, education of hospital staff about scrupulous hand washing, routine screening for vancomycin resistance among clinical isolates, contact isolation for patients with VRE such as single rooms or cohorting and strict wearing and removing gloves, and active rectal surveillance cultures. Despite the above infection control protocols, VRE is still endemic in most hospitals, and antibiotic overuse, non-compliance with preventive measures, insensitive detecting methods for VRE, and an increased influx of patients colonized with VRE into the hospitals could be possible causes[19].

Incidence of VRE infection in Neurosurgical practice

To our knowledge, this is first endeavored study in Korean Neurosurgical practice to systematically conduct documenting the epidemiology of VRE in a tertiary-care hospital. Reported VRE colonization rates among hospitalized patients vary widely, ranging from 1.5% to 32%, while the prevalence of VRE among non-hospitalized patients is 1-3.5%, usually involving non-epidemic isolates[11,14,20-22]. Futardo et al.[7] reported that the incidence of VRE in neurosurgical department was from 2% to 6%. In the present study, the data show a slightly higher incidence of 6.1% when study is confined to the ICU cohorts. Because there was no nation-wide study regarding incidence and prevalence of VRE specifically in NICU, we could not tell

or compare the implication of this value. In our hospital, the rate of VRE isolation was highest in our department for not totally understood mechanism, but the incidence tends to decrease since 2008 by active infection control program held by institutional CDC.

Among fifty-two patients with VRE colonization in the current study, 17 patients became infected during their ICU stay, whereas remaining 35 acquired positive VRE cultures either urine, blood or rectal swab while they were admitted on the general ward. The former patients generally showed more active form of infection manifested either by high relapsing fever, meningitis, sepsis or multi-organ failure, or blood-tinged stool. On the contrary, the latter patients seemed to be found incidentally in most instances, except one patient of active operative wound infection who required systemic linezolid. While most Western literatures stated high detection rate of VRE in rectal swab, this study pointed out a rather dormant form of urinary tract infection, mainly through Foley catheter.

Risk factors of VRE infection in Neurosurgical practice

The association between VRE colonization or infection and certain underlying medical conditions, e.g., diabetes mellitus, chronic renal failure, malignancies and transplantation, are well-known causes.[6,11] In the present study, medical co-morbidities were not significantly associated with VRE infection, except diabetes. This fact renders hypothesis of disturbed immunity and pre-existing angiopathy on the digestive tract. Pulmonary infection during ICU stay was another major determinant for VRE infection, and it was closely associated with longer period of mechanical ventilation. Use of steroids and antacids, dryness of trachea, retention of saliva in the mouth, and subsequent stress on the digestive tract can be possible explanations for this phenomenon.

The possibility that preceding antimicrobial treatment can be an important risk-factor for nosocomial VRE has been explored in numerous studies of both colonized and infected patients, but with conflicting results. In our department, third-generation cephalosporin is one of the most commonly prescribed antibiotics. Our study also showed that 40.4% of patients with VRE isolates previously used cephalosporin. Vancomycin was also given in 12 of 52 patients with VRE, due to methicillin-resistant *Staphylococcus aureus* (MRSA) isolation either from the sputum, or operative wound. In the NICU, almost all patients who underwent cranial procedures received third-generation cephalosporin for at least 7 to 10 days. If such patients suffered from other systemic infection in this period, vancomycin or anti-anaerobic agents should be provided. Whether to decide start or quit other antibacterial agents is not entirely simple or straightforward in practical sense. In spite of this, the result suggests that appropriate use of specific cephalosporin and vancomycin in terms of dosage and period, should be recognized and commanded to minimize nosocomial VRE colonization or infection[8,19].

Prolonged hospitalization and direct admission to ICU were also associated with higher VRE colonization rate[12]. These results simply reflect an increased severity of illness in the population studied. Patients with lower GCS score on admission were more associated with intensive treatment. Sixty-five percent of patients with VRE colonization had a lower GCS score less than 8. Both unconsciousness, total dependency with medical staffs, and weakened self-defense mechanism are prone to be infected by opportunistic pathogens. In a similar sense, numerous catheters placed in the patients, including central venous catheter, nasogastric tube, Foley catheter, lumbar drain, and operative drainage bags altogether play a critical role in evoking skin contamination of secondary bacterial infection. Earlier removal of drains, dry dressing with washed hands, meticulous wearing and removal of gloves and regular swab should be followed by medical personnel, either resident, intern physicians, or nursing staffs. Assessing the pattern of pathogen isolation is also prerequisite to eradicate nosocomial infection mainly made by staffs.

Segregation of VRE-positive patients into an isolating room is important and effective to prevent contagious spread. One patient in a single room is a most efficient way to isolate. Gathering two or more patients in one room is not recommended, because this makes vicious cycle by allowing continuous contamination each other, and renders eradication of VRE impossible. In present time, the available treatment option is to isolation of such patient from non-contaminated patients and direct discharge to home, only if patients show subclinical or latent infection. Byers et al.[3], starting from an outbreak of VRE, insisted that by implementing the measures recommended by the CDC, they were able to significantly reduce the dissemination of the pathogen in the hospital.

This study has some limitations including retrospective analysis in a single institute, excluding significant patient population for some reasons, insufficient consensus of definition, lack of protocols to control infection, absence of consideration for MRSA, and focus to specific postoperative infection. However, this study at least showed the real situation of confronting VRE infection in ICU setting. Further study will be mandated to set a standard guideline to control evolving super-infection in near future.

The additional guideline for prevention of VRE in Hanyang University Medical Center

Additionally to The CDC guideline, automatic antibiotics restriction order system (notifying system to the clinician) for discontinuing inappropriate or wrong antimicrobial therapy was introduced in our hospital. This system was somewhat associated with decreasing the duration of antibiotics use and encouraging correct antibiotics use. Alcoholic hand rinse dispensers were placed at all entrance of each sick room since 2007. This could have resulted in improving hand hygiene practices with a subsequent decrement of patient-to-patients spread of VRE.

CONCLUSION

A VRE is a pathogen with progressively increasing incidence in our environment. Compared to the non-specific Western literatures, our study showed some peculiar findings of high prevalence of VRE in neurosurgical patients with low GCS score, longer urinary catheter placement instead of rectal contamination, longer ICU stay, and presence of next to bed VRE-positive patients, meaning incomplete patient segregation. Although not reached in statistical senses, we should be still careful of appropriate use of antibiotics such as vancomycin, third-generation cephalosporin, and multiple antimicrobial agents. In addition to these, by careful hand washing with antiseptics, strict glove and gown handling, meticulous and active screening, and complete segregation can protect outburst of VRE colonization. To ensure early detection and containment of VRE, a more targeted, systematic approach is needed among patients at risk from VRE disease in neurosurgical department.

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